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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,607	10/23/2001	Lino Tavares	208.1004US	1029

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EXAMINER
GHALI, ISIS A D

ART UNIT	PAPER NUMBER
1615	11

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/045,607	Applicant(s) TAVARES ET AL.	
	Examiner Isis Ghali	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16 and 20-45* is/are pending in the application.

4a) Of the above claim(s) *39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,20-38 and 40-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' amendment A and the letter, both filed 08/25/2003.

Claims 17-19 have been canceled.

Response to Election/Restrictions

1. The election of species of the transdermal system and the election of species of the backing layer have been withdrawn.

2. Applicant's election without traverse of Group I, claims 1-16, and 20-45, and species (a) of the polymer, in Paper No. 8 is acknowledged.

3. Claim 39 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species of the polymer, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Claims 1-16, 20-38, 40-45 are included in the prosecution.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 35 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 35, the expression “rubber-like polymer” does not set out the metes and bounds of the claim. Recourse to the specification does not define the expression “rubber-like polymer”. Clarification is requested.

Claim 44 recites the limitation "softening ester" in claim 23. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-16, 20-38, 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,910,205 ('205).

US '205 teaches a transdermal delivery system of loratadine for the treatment of allergic conditions (abstract). The system is formed of patch applied to skin for a specific period of time to permit the penetration of a desired amount of loratadine through the skin. The patch will be worn for one to four days and provides a total daily dose of 0.5 to 5 mg (col.2, lines 28-34). The patch comprises a reservoir having 10-20% loratadine; 50-60% solvent; and 20-35% fatty acid esters, i.e. softening agents (col.2, lines 19-29). The patch further comprises a backing layer and a release liner (col.2, line 64; col.3, line 6). The patch delivers 2.26 mg/15cm^2/day of loratadine (Table I). The reference disclosed that the dose may be varied depending on the size and age of the patient, and may also depends upon the severity of the condition being treated (col.3, lines 56-60). The frequency of dosage application can be once every 3 days once every 7 days (col.4, lines 5-10).

The reference does not teach the specific delivery profile of loratadine, the specific amounts of different ingredients, or specific solvents and softening agents in the transdermal delivery system.

The claimed amounts of different ingredients in the reservoir layer do not impart patentability to the claims because it is within the skill in the art to select optimal parameters in order to achieve a beneficial effect. Thus, the claimed amounts of the drug, solvent and the softening agent are not considered critical, absent evidence to the contrary.

The selection of particular solvent and softening agent for a specific drug is within the skill of the art depending on the properties of the each drug and its intended use. Thus the solvents and softening agents claimed in claims 37, 38, 44, and 45, do not impart patentability to the presented claims, absent evident to the contrary.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal device to deliver loratadine to treat allergic conditions as disclosed by US '205, and adjust the dose to deliver a specific desired plasma profile according to the patient's need, motivated by the teachings of US '205 that the dose may be varied depending on the size and age of the patient, and may

also depends upon the severity of the condition being treated, with reasonable expectation of having a transdermal drug delivery device that delivers loratadine at the desired levels and treats allergic conditions effectively.

9. Claims 1-16, 20-38 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,103,735 ('735) in view of US 5,091,186 (186).

US '735 teaches a pharmaceutical composition useful for treating allergic rhinitis comprising loratadine (abstract; col.5, line 66). The composition can be administered in the form of transdermal patches (col.7, lines 8-10).

The reference does not teach the specific delivery profile claimed by the applicants as claimed in claims 1-16. The reference does not teach the structure of the transdermal delivery system as claimed in claims 20-38 and 40-45.

US '186 teaches a transdermal drug delivery device to deliver drugs at therapeutically effective rates for about 20-28 hours (abstract; col.6, lines 4-20; col.7, lines 29-40). The reference teaches the antihistaminic as one of the drugs to be delivered by the transdermal delivery device (col.5, line 10). The transdermal device comprises a flexible backing layer, an adhesive drug reservoir layer, and a release liner (col.3, lines 25-30, 6-63; col.4, line 43). The delivery profile of the drug is determined by the diffusivity of the drug in the reservoir layer, the solubility of the drug in the reservoir layer, and the degree of drug loading (col.6, lines 24-44). A given drug loading value will provide certain duration of delivery rate (col.7, lines 18022). To achieve the known desirable blood level of the drug, the delivery rate of the drug ranges from 10-50

ug/cm^2/hr (col.7, lines 47-51). The reservoir is pressure sensitive adhesive comprising rubbers, polysiloxane and polyurethanes (col.4, lines 33-40). The reservoir further comprises solvent and glycol, claimed by applicant as softening agent (col.6, line 1; col.7, line 55).

The claimed amounts of different ingredients in the reservoir layer do not impart patentability to the claims because it is within the skill in the art to select optimal parameters in order to achieve a beneficial effect. Thus, the claimed amounts of the drug, solvent and the softening agent are not considered critical, absent evidence to the contrary.

The selection of particular solvent and softening agent for a specific drug is within the skill of the art depending on the properties of the each drug and its intended use. Thus the solvents and softening agents claimed in claims 37, 38, 44, and 45, do not impart patentability to the presented claims, absent evident to the contrary.

The determination of the relative release rate via an in-vitro permeation test utilizing a Valia-Chien cell is known in the art and it is not part of the claimed method of treating allergic rhinitis; or even a part of the transdermal device that provide particular plasma levels of loratadine. It is only an in-vitro diagnostic test that is expected to provide the same results obtained from two similar delivery devices tested under the same circumstances, and the recitation of this in-vitro test does not impart patentability to claims directed to method of treating allergic rhinitis or claims directed to transdermal device applied to patients to provide specific plasma levels of loratadine, i.e. in vivo use.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using a transdermal device comprising loratadine, as disclosed by US '735, and provide the loratadine in the transdermal device disclosed by US '186 that provide a particular delivery profile of the drug, and manipulate the amount of the drug to obtain the desired delivery profile, motivated by the teaching of US '186 that a given drug loading value will provide a certain duration of delivery rate depending on the drug loading, with reasonable expectation of having a transdermal drug delivery device to deliver loratadine to treat allergic rhinitis effectively.

10. Claims 37, 38, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '205 in view of US 5,240,711 ('711).

The teachings of US '205 are discussed above.

The reference does not teach the specific solvents and softening agents and their amount.

US '711 teaches a transdermal drug delivery device for controlled delivery of drug comprising backing layer, polymeric reservoir and protective liner. The reservoir comprising: 20-90% of polymeric material, 0.1-20% of the drug, 0.1-30% softener, and 0.1-30% of solvent (abstract; col.1, line 64-67; col.4, line 23). The reservoir is pressure sensitive adhesive and contains rubber-like co-, homo-, or block-copolymers (col.3, lines 25-26). The solvents used include those contain at least one acidic group, monoesters of dicarboxylic acids, such as monoethyl glutarate (col.4, lines 13-16). The softeners include medium chain triglycerides of the caprylic/capric acids or coconut oil;

and dodecanol (col.3, lines 63-68; col.4, lines 1-2; col.7, lines 25-29). The backing is flexible, inflexible or aluminum foil (col.7, lines 5-12).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic conditions using a transdermal device comprising loratadine that provides a specific delivery profile and having particular structure as disclosed by US '205, and select the specific solvents and softening agents disclosed by US '711, motivated by the teaching of US '711 that the transdermal device having these particular ingredients in its reservoir layer provides a controlled delivery of the drug, with reasonable expectation of having a transdermal drug delivery device to deliver loratadine to treat allergic conditions effectively.

11. Claims 37, 38, 44, and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '735 in view of US '186 as applied to claims 1-16, 20-38 and 40-45 above, and further in view of US '711.

The teachings of US '735, US '186 and US '711 are discussed above.

The combination of US '735 and US '186 does not teach the specific solvents and specific softening agents as claimed in claims 37, 38, 44, and 45.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat allergic rhinitis using a transdermal device comprising loratadine that provides a specific delivery profile and having particular structure, and select the specific solvents and softening agents disclosed by US '711, motivated by the teaching of US '711 that the transdermal device having these particular ingredients in its

reservoir layer provides a controlled delivery of the drug, with reasonable expectation of having a transdermal drug delivery device to deliver loratadine to treat allergic rhinitis effectively.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 5,045,319 disclosed transdermal delivery system to deliver pharmaceuticals wherein the in-vitro release studies can be conducted using Valia-Chien diffusion cell.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (703) 305-4048. The examiner can normally be reached on Monday through Thursday from 7:00 AM to 5:30 PM, Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.

Isis Ghali
Examiner
Art Unit 1615

Isis Ghali.

ISIS GHALI
PATENT EXAMINER